

## NON-EXPANDED POROUS POLYTETRAFLUOROETHYLENE (PTFE) PRODUCTS AND METHODS OF MANUFACTURE

### FIELD OF THE INVENTION

[0001] The present invention relates to non-expanded porous polytetrafluoroethylene (PTFE) products and methods of manufacture. The present invention further relates to medical devices such as grafts, endoprosthesis or intraluminal devices, which include as a component a non-expanded porous PTFE material. The non-expanded porous PTFE material is formed from an extruded mixture of PTFE resin and an extractable polymer material, the polymer material being extracted to leave voids or pores in the extrudate. Implantable tubular grafts, stent coverings, medical patches and fabrics can be made in this manner. Thin stent coverings can be applied on the exterior surface of the stent, on the interior surface of the stent, or both.

### BACKGROUND OF THE INVENTION

[0002] Porous PTFE is conventionally formed from a mixture of PTFE particles and lubricant which is pre-processed to form a compacted billet, extruded into a particular shape, such as a tube, and stretched or expanded to provide a node and fibril structure. Such a node and fibril structure not only imparts certain physical properties to products made therefrom, but also provides porosity to the products. Once stretched it is referred to as expanded PTFE (ePTFE). Sintering of the ePTFE is then generally carried out to "lock in" the porous structure. In applications involving medical implants, such as grafts, stent-grafts, patches and other such products, expanded PTFE has provided appropriate porosity to allow assimilation of the implant by the body and tissue ingrowth into the porous wall, both of which are necessary for long term patency.

[0003] The formation of ePTFE requires a great deal of expertise and costly equipment. Parameters such as the ratio of lubricant to PTFE particles in the feed material, the pressure and



rendered insoluble by increasing the pH. The biodegradable material within the pores is intended to encourage ingrowth and be absorbed by the body over time.

[0007] U.S. Patent No. 5,840,775 discloses a process for making porous PTFE by contacting PTFE with a fluid which penetrates and swells, but does not dissolve the PTFE. The fluid is introduced using temperature to permit extensive penetration of the PTFE. The liquid is then removed to leave a swelled, open structure of PTFE. As previously mentioned, expanded PTFE has been used extensively for grafts and stent-graft devices. Expanded PTFE covers and/or liners for stents have found to be particularly useful in endoprosthetic devices because while the porosity of the PTFE allows for assimilation of the device by the body, it also prohibits unwanted hyperplasia.

[0008] Endoprosthesis devices including stents, stent-grafts, grafts, vena cava filters, balloon catheters, and so forth, are placed or implanted within various body vessels for the treatment of various diseases. One particular type of an endoprosthesis device is the stent. A stent is implanted within a vessel for the treatment of stenoses, strictures, or aneurysms in the blood vessels. The devices are implanted within the vascular system to reinforce diseased, partially occluded, weakened or abnormally dilated sections of the blood vessel. Stents are often employed after angioplasty to prevent restenosis of a diseased blood vessel. While stents are most notably used in blood vessels, they have also been implanted in other bodily vessels including urinary tracts and bile ducts to reinforce and prevent neoplastic growth.

[0009] Stents are typically longitudinal tubular devices formed of biocompatible materials and come in a variety of construction types, and are often expandable in nature. Many if not all of the materials used for stents involve metal or carbon fiber materials which are highly electro-positive and are bio-active. Since stents tend to be used under conditions where they are counteracting disease processes, supporting healing processes, or guarding against stenosis of a passage, bio-activity, which may encourage undesirable or poorly regulated growth processes, or lead to clot formation, should be avoided.

[0010] Coating of the stent can keep the stent from directly contacting surrounding tissue or fluids, and thus can theoretically protect against unwanted electrochemically induced tissue reactions.

[0011] In the field of expandable stents, a further problem arises due to the fact that many stent constructions involve structures that have numerous apertures or spaces between various strands or structural elements of the stent such as those structures that are filamentous, wire-like, or of a tubular nature in which various openings have been cut or etched into the stent. With these constructions, tissue may grow through the openings of the stent. Furthermore, the stent itself may provoke a foreign body reaction and be both a stimulus for and a framework supporting, proliferative tissue growth, resulting, for example, in scar tissue or restenosis of the very region it is placed to control.

[0012] One approach to this drawback is to provide a coating, liner, cover or both, for the stent which prevents the healing or diseased layer of tissue from directly contacting the stent, or from passing through the stent in any way. Such liners may be formed, for example, of porous polytetrafluoroethylene (PTFE) which allows the passage of fluids and vital materials while serving as a barrier to tissue growth. However, when applying such a construction, a further difficulty which may arise is that the layer or sleeve of polymer must be attached to the stent for example, by staples or sutures at one end, or is prone to developing loose pockets or folds which might accumulate organic matter or lead to sepsis or unusual growth. Also, the necessarily thin liner material may detach or degrade. The risk of loose or unattached liner material is particularly great for constructions which utilize poorly adherent polymers, such as PTFE, or structures which seek to combine an expandable stent of stiff material, which changes both its dimension and its shape, with a dissimilar liner or shell.

[0013] One method for overcoming these problems is found in U.S. Patent No. 6,010,529 in which tube of polymeric material, e.g. expanded polytetrafluoroethylene (ePTFE), is passed through the interior of a stent body and is turned back upon itself over the stent to form a cuff. The assembly is then heated and the outer layer contacts and coalesces with the inner layer,

closely surrounding the stent body within a folded envelope having a continuous and seamless end. Porosity is imparted to the PTFE by previous stretching or expansion the material.

[0014] Another type of covered stent which permits radial expansion is shown in WO 96/00103. As shown and described therein, a metallic expandable stent includes an outer covering of ePTFE. The ePTFE cover exhibits suitable expansion capabilities so as to enable the cover to expand upon expansion of the underlying stent. A polytetrafluoroethylene/lubricant blend may be extruded into a tube and the tube heated to remove the lubricant. Then, in order to impart the expandable characteristics to the ePTFE cover during formation of the ePTFE cover material, the ePTFE must undergo successive processing steps of expanding the material, sintering the material, radially dilating the material and resintering the dilated material, a procedure that is quite process intensive. The device described therefore requires precise manufacturing techniques and is extremely processing sensitive. Careful processing of the material forming the cover is required in order for the cover to exhibit sufficient expansion capabilities.

[0015] U.S. Patent No. 5,824,046 describes a composite intraluminal device, in particular an elongate radially expandable tubular stent having an interior luminal surface and an opposed exterior surface extending along a longitudinal stent axis. A stent cover is formed of unsintered ePTFE which is expandable.

[0016] There remains a need in the art to produce porous PTFE material which can be used in a variety of products and applications, and particularly in medical device applications, without requiring expansion to produce porosity. There is also a need for producing such porous PTFE materials without the extensive costs and technical difficulties associated with conventional porous PTFE having a node and fibril structure produced using expansion techniques. Moreover, there is a need for a stent-graft composite device incorporating such a porous material.

## SUMMARY OF THE INVENTION

[0017] In one aspect of the present invention there is provided an endoprosthesis device which includes a tubular extrudate having a PTFE matrix and distributed therein discrete domains of an extractable polymeric material, wherein upon exposure to sufficient dissolving medium or degradation temperature said discrete domains are extracted from said matrix to create pores in said tubular extrudate.

[0018] In another aspect of the present invention there is provided a vascular graft comprising the aforementioned porous tubular extrudate.

[0019] In another aspect of the invention there is provided a method of forming a porous PTFE product which includes the steps of: providing a mixture of PTFE resin and an extractable polymer material; extruding said mixture to form an extrudate which includes a PTFE matrix with discrete domains of said extractable polymer material; subjecting said extrudate to a solvent for said extractable polymer material, a temperature sufficient to degrade said extractable polymer material or a combination thereof, whereby at least a portion of said extractable polymer material is extracted, thereby forming pores in said extrudate.

[0020] In another aspect of the invention there is provided a stent-graft composite product, whereby the stent is radially distensible and has a cover, a liner or both at least partially covering the stent structure and being made from the porous PTFE material of the present invention. The stent can be affixed to the porous PTFE cover by any suitable means, including using adhesives, laminating inner and outer coverings through the stent openings, sutures, pockets or cuffs, or other such means.

[0021] Although the formation of pores in the products of the present invention are formed without expansion techniques, such porous PTFE materials may be subsequently subjected to conventional expansion and sintering processes.

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[0022] In another embodiment of the endoprosthesis device of the present invention there is included an elongate radially expandable tubular stent having an interior surface and in exterior surface extending along a longitudinal stent axis. The expandable tubular stent has a stent cover on said interior surface, exterior surface or both, the cover being formed of a porous polytetrafluoroethylene. The porous polytetrafluoroethylene cover is a non-stretched (non-expanded) porous structure, the non-stretched structure lacking node and fibril structure.

[0023] In particular, the present invention relates to a radially expandable stent for use in treating stenoses wherein the stent is at least partially covered with an expandable polymer covering which includes the porous PTFE of the present invention and which physically isolates the stent from surrounding blood and tissue.

[0024] In one desirable embodiment of the present invention there is included a porous PTFE which is prepared by extracting siloxane from an interpenetrating network (IPN) of PTFE and siloxane, leaving behind a porous PTFE structure without having to expand and stretch the PTFE.

## BRIEF DESCRIPTION OF THE DRAWINGS

[0025] Fig. 1 is a perspective view of one type of intraluminal stent device that may be used in the present invention.

[0026] Fig. 2 is a perspective view of a different intraluminal stent device which may be used in the present invention.

[0027] Fig. 3 is a perspective view of a stent-graft device which employs the intraluminal stent device of fig. 1 in combination with a porous polytetrafluoroethylene cover of the present invention on both the inner and outer surface of the device.

[0028] Fig. 4 is a cross-sectional view of the same stent-graft device shown in Fig. 3.





medium may be delivered with sufficient heat if necessary to maximize the ability to remove the polymeric domain. In some instances, such as when water or other medium which does not wet well the surface of PTFE, is used as the dissolvable medium, it may be necessary to include force, e.g. pressure or a combination of heat and force to penetrate to the polymeric domains.

[0040] Table I below provides a non-exclusive list of useful extractable polymeric components and selected solvents for their removal.

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TABLE I	
Selected Extractable Polymers	Selected Useful Solvents
polyvinyl alcohol (PVA)	water, methanol, ethyl alcohol
cellulose triacetate	acetone
poly(oxyethylene glycols)	water, toluene
ethyl cellulose	ethanol, isopropanol, methylacetate
methylcellulose	cold water
cellulose propionate	acetone, dioxane
carboxymethylcellulose	water
dextran (glucose polymer)	water
agar (poly(D-galactopyranose))	hot water
poly(vinylformal)	chlorinated solvents, aliphatic hydrocarbons
poly(sodium acrylic acid)	water
poly(sodium methacrylic acid)	water
sugar (polysaccharides)	water
polyvinylacetate	methanol, ketones, esters, chlorinated hydrocarbons, aromatic hydrocarbons
polystyrene	toluene
gelatin	water
wheat (prolamines) (simple proteins)	75% alcohol
poly(vinylpyrrolidone)	water, organic solvents
poly(ethyleneterephthalate)	trifluoroacetic acid, o-chlorophenol, hexafluoroisopropanol, various phenolics, phenol (cresol)
polyacrylonitrile (PAN)	dimethylformamide (DMF), dimethylsulfoxide (DMS), dimethylacetamide (DMAC), ethylene carbonate, propylene carbonate, adiponitrile, $\gamma$ -butyrolactone
poly(methacrylate) (PMA) and poly(methylmethacrylate) (PMMA)	acetonitrile, isovinyl acetate, n-butylchloride, heptanone-4, heptanone-3, n-propanol
poly(oxymethylene)	phenol (109°C) aniline (130°C) ethylene carbonate (145°C)
poly(acrylic acid)	alcohols, formamide, dimethylformamide
poly(acrylamide)	morpholine, water
nylon 6	m-cresol, acetic acid, trichloroacetic acid
nylon 6,6	formic acid, trifluoroethanol, chloral hydrate, dimethylsulfoxide (DMSO), formamide, acetic acid, chloroacetic acid
nylon 6,10	chlorobenzene
nylon 11	dimethylformamide, dimethylsulfoxide
nylon 18	dimethylformamide, dimethylsulfoxide, pyridine

[0041] In addition to water, organic solvents and other dissolving medium being employed to extract the polymer, the application of heat can be applied to cause the polymer to flow out of the PTFE matrix or to degrade the polymer such that it can be removed, for example, by subsequent dissolving medium. Additionally, electromagnetic radiation may be employed as a means of removing the polymer. Electron beam radiation is possible, but other forms may also be employed depending on the polymer.

[0042] In cases where the polymer is a crosslinked polymer, e.g. a thermoset polymer, solvent dissolution may be difficult and degradation of the polymer may be a first step in its removal. In the case of thermoplastic polymers, extraction via solvents or heat is generally preferred. The molecular weight of the chosen polymer may vary extensively and its lower and upper ranges are only limited by practical concerns such as availability, difficulties in forming a blend with PTFE resin or difficulty in extraction.

[0043] It is generally known that PTFE resin has a density of 2.2 g/cc. As a result of undergoing the process of the present invention, porous, non-expanded PTFE products are formed having a bulk density desirably in the range of about 0.2 to about 0.5. Thus, a substantial amount of air space or porosity has been introduced into the PTFE material. The lower limit of porosity is governed by the need to establish sufficient ingrowth or acceptability in the body. The upper limit is governed by the need to maintain structural integrity of the porous PTFE product. Thus, a wide range of porosity is possible within these guidelines.

[0044] Porous, non-expanded PTFE products, and in particular non-expanded porous PTFE grafts are made in accordance with the present invention. These grafts may be used alone as surgical implants or combined with a supporting structure, such as a radially distensible stent, to form a stent-graft. Such stent-grafts are generally used as intraluminal devices, particularly in vascular applications.

[0045] The present invention provides a covered stent which may be implanted intraluminally within a body vessel and disposed adjacent an occluded, weakened or otherwise

damaged portion of the vessel so as to hold the vessel open. The covered stent is typically delivered intraluminally via a balloon catheter. The device is delivered in a compressed condition and once properly positioned may be deployed by radial expansion. The most common form of deploying the intraluminal device is by balloon expansion, however, the present invention may also be deployed by use of a self-expanding stent.

[0046] The stent may be made from a variety of materials including stainless steel, titanium, platinum, gold and other bio-compatible metals. Thermoplastic materials which are inert in the body may also be employed. Shaped memory alloys having superelastic properties generally made from specific ratios of nickel and titanium, commonly known as nitinol, are among the preferred stent materials.

[0047] Various stent types and stent constructions may be employed in the invention. Among the various stents useful include, without limitation, self-expanding stents and balloon expandable <sup>stents</sup> ~~extents~~. The stents may be capable of radially contracting, as well and in this sense can best be described as radially distensible or deformable. Self-expanding stents include those that have a spring-like action which causes the stent to radially expand, or stents which expand due to the memory properties of the stent material for a particular configuration at a certain temperature. Nitinol is one material which has the ability to perform well while both in spring-like mode, as well as in a memory mode based on temperature. Other materials are of course contemplated, such as stainless steel, platinum, gold, titanium and other biocompatible metals, as well as polymeric stents.

[0048] The configuration of the stent may also be chosen from a host of geometries. For example, wire stents can be fastened into a continuous helical pattern, with or without a wave-like or zig-zag in the wire, to form a radially deformable stent. Individual rings or circular members can be linked together such as by struts, sutures, welding or interlacing or locking of the rings to form a tubular stent. Tubular stents useful in the present invention also include those formed by etching or cutting a pattern from a tube. Such stents are often referred to as slotted

stents. Furthermore, stents may be formed by etching a pattern into a material or mold and depositing stent material in the pattern, such as by chemical vapor deposition or the like.

[0049] Fig. 1 illustrates an intraluminal device in the form of a stent 12. Fig. 2 illustrates an intraluminal device in the form of a stent 5 having a different construction than that shown in fig. 1.

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[0050] ~~Fig. 3 illustrates generally at 10 an intraluminal device in the form of a stent 12 as shown in fig. 1 having a cover 14 on the outer surface 12 and liner 16 on the inner surface, both of which may be of the porous structure shown below in fig. 7. The stent may optionally have only a cover 14 as shown in fig. 5, or only a liner 16 as shown in fig. 6, or both as shown in fig. 3. In a preferred embodiment, the stent has both a cover 14 and a liner 16. The liner, cover, or both, will be referred to hereinafter collectively as a cover or covering. The cover provides an effective barrier about the stent 12 preventing excessive cell or tissue ingrowth or thrombus formation through the expanded wall of the stent 12.~~

[0051] Fig. 4 is a cross-sectional view of the same device as shown in fig. 3 with a cover 14 and a liner 16 around stent 12.

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[0052] ~~Fig. 1 is a more detailed illustration of stent <sup>12</sup>10 and shows generally an elongate tube. The body of stent 12 defines an opposed interior surface 11 and an exterior surface 13 and is formed of a generally open configuration having a plurality of openings or passages provided for longitudinal flexibility of the stent as well as permitting the stent to be radially expanded once deployed in the body lumen. Both the interior surface 11 and the exterior surface 13 may have the porous PTFE covering of the present invention. On the interior surface the covering is referred to as the liner <sup>16</sup>12 as shown in Fig. 1 and on the exterior surface it is referred to as a cover 14 as shown in Fig. 1.~~

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[0053] While the figures illustrate a particular construction of stent 10, one of skill in the art would recognize that the porous PTFE covering material as described by the present

invention would find utility in any stent configuration, and in particular the open stent configurations.

[0054] Stent 12 may be employed in combination with a cover 14 or liner 16 but is preferably employed with both. The cover 14 may be applied over the tubular stent 12 so as to fully circumferentially surround the stent 12, while the liner 16 is applied inside and through the stent 12 so that the stent 12 fully circumferentially surrounds the liner 16.

[0055] In one particular desirable embodiment of the present invention, the porous polytetrafluoroethylene (PTFE) material useful herein is first obtained in the form of an interpenetrating network of PTFE and a siloxane. In particular, polydimethylsiloxanes have been found to be useful. The silicone is then extracted from the IPN using either thermal or chemical means. The removal of the silicone leaves behind a porous PTFE structure. A particular material for use herein is Silon®, an interpenetrating polymer network (IPN) of polytetrafluoroethylene (PTFE) and polydimethylsiloxane (silicone) supplied by Bio Med Sciences, Inc. located in Bethlehem, PA. Such IPN polymer networks are described in U.S. Patent No. 6,022,902 incorporated by reference herein in its entirety. In this patent, Silon® is described as a breathable, hydrophobic polysiloxane membrane reinforced with poly(tetrafluoroethylene).

[0056] Fig. 7 shows a three-dimensional representation of an extrudate 40 which includes a PTFE resin matrix 42 having distributed therein discrete extractable polymeric domains 44. Such an extrudate may be extruded into a variety of shapes. Desirably, it is rolled or extruded into either a flat sheet, which is then formed into a tubular structure for use as a graft or in a stent-graft device, or alternatively it is directly extruded into tubular form 14 as shown in Fig. 5.

[0057] The removal of the extractable polymeric component from the IPN leaves behind a porous PTFE structure without having to go through the added steps of stretching or expanding the PTFE in order to obtain the porous structure. Quite obviously, this simplifies the manufacturing process by decreasing the number of steps required, and also increases efficiency.

As previously described, porous PTFE often requires the expanding and stretching steps in order to achieve the desired porous structure. Fig. 7a illustrates generally at 20 a porous PTFE structure after removal of the extractable polymeric component. The removal of the polymeric domain leaves behind the porous structure wherein voids or pores 25, are found distributed within matrix PTFE 30.

[0058] The novel porous PTFE structure produced by the present inventive process is quite different from the porous structure produced by PTFE which has been stretched, or expanded. Typically, PTFE which has been stretched (ePTFE) has a node and fibril structure as seen in Figure 8. After stretching, the ePTFE possesses nodes 32 connected to fibrils 34. The spaced in between the nodes and fibrils represent pores 36.

[0059] When the extractable polymeric component is a siloxane, removing the siloxane from the IPN PTFE matrix of siloxane/PTFE through the use of heat involves heating the IPN structure to temperatures of between about 300°C and about 390°C. Alternatively, chemical removal of the siloxane may be accomplished using a compound selected from the group consisting of toluene, heptane, chloroform.

[0060] Sintering is typically accomplished at or above the crystalline melting point of PTFE. It refers to the bonding of particles in a mass by molecular (or atomic) attraction in the solid state through the application of heat below the melting point of the polymer. Sintering causes the strengthening of the powder mass and normally results in densification and often recrystallization.

[0061] A PTFE tube may be extruded as a tube from an extrusion device, or extruded as a film and subsequently wrapped into a tube. Extrusion techniques of PTFE are well known in the art.

[0062] As discussed above, the stent may be covered on the interior surface 11 of the stent 10, the exterior surface 13 of the stent 10, or both. Preferably, the stent 10 is covered on

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both the interior 11 and the exterior 13 surfaces of the stent <sup>112</sup>10. Having the entire surface of the stent <sup>112</sup>10 covered with the porous PTFE of the present invention provides an effective barrier about the stent <sup>112</sup>10 preventing excessive cell or tissue growth, or thrombus formation through the expanded wall of a tubular stent <sup>112</sup>10.

[0063] In order for the covering of porous PTFE to function effectively in combination with an expandable stent, the material must exhibit sufficient expansion characteristics so as to enable the stent cover to open or expand along with the radial expansion of the stent 10. If the covering is applied to the stent in its fully deployed state, and then folded during insertion, it may only require unfolding as the stent radially expands. The porous, non-expanded PTFE covering may additionally be subjected to expansion prior to attachment to the stent, or alternatively be affixed to the stent in the radially compressed state and expanded during the expansion of the stent. If the covering material does not effectively open or expand with the stent, several problems can arise. The covering material may tear, and may even detach from the surface of the stent if improper or dissimilar expansion of the covering material occurs with the expansion of the stent.

[0064] In order to improve the adhesion, and further prevent detachment of the PTFE covering from the stent, the PTFE may be fused or welded around or to the metal stent. This may be accomplished either through a heating process and/or bonding process. If heating is utilized, typically the PTFE will be heated above its sintering temperature.

[0065] If an adhesive is utilized, preferably a biocompatible adhesive is used. Such adhesives are known to one of skill in the art and include, for example, polyurethanes, epoxies, cyanoacrylates, polyamides, polyimides, silicones, and so forth. Dispersions of PTFE or FEP (fluoroethylpropylene) may also be utilized. This list is not exclusive and is intended for illustrative purposes only, and is in no way intended as a limitation on the scope of the present invention. There is a vast number of adhesives that can be used for such applications, limited by their biocompatibility, and by their ability to bond to polymeric materials (e.g. PTFE) and metals, particularly in aqueous environments.

